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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/739,933 | 12/18/2000 | James Steven Reid | 07306-021001 | 4882 |

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| EXAMINER | |
|---|---|
| TURNER, SHARON L | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1647 | 27 |

DATE MAILED: 12/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/739,933 | REID ET AL. | |
| | Examiner | Art Unit | |
| | Sharon L. Turner | 1647 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *9-15-03*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-3,5-8,20,33,63 and 64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-8,20,33,63 and 64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8-27-03*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9-15-03 has been entered.

2. Claims 4, 9-19, 21-32 and 34-62 are canceled. Claims 1-3, 5-8, 20, 33 and 63-64 are pending.

**Election/Restriction**

3. Applicant's election with traverse of Group I, claims 1-8, 16, 20, 27 and 33 in part to the extent drawn to TGF-ALPHA-α, second compound that inhibits a naturally occurring signal that inhibits migration and neurodegenerative disease, in Paper No. 13 is acknowledged. The traversal is on the ground(s) that the search and examination of the different inventions and species would not be burdensome or unreasonable. This is not found persuasive because the methods are distinct as they are comprised of different steps, utilize different reagents and achieve distinct results as claimed. Thus, a search for one of the methods or species would not be co-extensive with a search for any other method or species.

The requirement is still deemed proper and is therefore made FINAL.

***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 2, 3, 5 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites particular administration in vivo to an individual. However, claim 20 specifies that the CNS tissue is in tissue culture and thus the administration is not apparently in vivo. Applicant's should clarify the metes and bounds of the claim with respect to the in vitro culture. For example, it is unclear whether applicant's intention is either to claim a method that provides for the in vivo administration and then explantation of particular tissues to culture, or whether applicant's intention is to administer directly to tissue culture. Further, it is unclear how applicant's intend the functional limitations of claim 1 to apply to the in vitro cultures as they are not apparently of in vivo specimens. Applicants may wish to consider an independent claim.

Claims 2, 3, 5 and 20 recite the limitation "the compound" in reference to claim 1. There is insufficient antecedent basis for this limitation in the claim.

***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1-3, 5-8, 20, 33, and 63-64 are rejected under 35 U.S.C. 103(a) as being anticipated by Weiss et al., 5,980,885, filed June 7, 1995 and issued Nov. 9, 1999.

Applicants note that their invention requires lesion or damage in addition to administration outside of the ventricles. Applicant's note that administration to the ventricles is not effective to provide for attraction of neural progenitor cells as claimed. Applicant's argue the previous 102 rejection of record citing that Weiss fails to teach or suggest administration of TGF-alpha outside the ventricles to an individual having CNS damage or lesion.

Applicants arguments have been fully considered but are not persuasive. While it is true that Weiss directs that a preferred embodiment of the invention is delivery of the growth factor to the ventricles, the Examiner notes that Weiss is not limited to a teaching of administration to the ventricles. Moreover, Weiss is directed to administration to patients with damage or lesion and for the purpose of attraction of neural progenitor cells to a site of damage or lesion in the CNS.

While the Weiss patent fails to ipsis verbis teach administration of TGF-alpha, "outside the ventricles," via, "intrastriatal administration," and wherein the site is, "spinal cord tissue and spinal nerve root origins," such limitations are anticipated by the reference.

Weiss et al., teach administration of TGF-α to patients in vivo for the purpose of inducing in vivo proliferation, migration and differentiation of neural and/or glial cell precursors and for treatment of injuries and diseases of the nervous system including Huntington's, Alzheimer's, Parkinson's and other neurological disorders, see in

particular Abstract, lines 5-7, column 25, line 20-column 26, line 64 and Examples 27-30. In addition, the method may be used in areas of demyelination or autoimmune disease such as MS for proliferation of glial schwann, see in particular columns 24-25. The method is also disclosed for use in the replacement of neurons, for example as transplants or grafts, disclosed at column 23. Weiss further teaches that these effects may be achieved by direct administration, thus obviating particular problems associated with transplant, see in particular column 12-25 in regard to culture, modification and transplantation of cells and columns 25-29 for the alternative method of direct administration for production of the appropriate cells and treatment in vivo. The cells so produced may be generically used to replace damaged or missing neurons and/or glia, see in particular Abstract and column 25, lines 34-41. In particular Weiss teaches injection of growth factors to animals having CNS damages or lesion, see in particular column 22, lines 10-17. The method as amended is also directed to an individual having CNS damage or lesion. Weiss teaches administration to patients suffering from injury or damage to the CNS and for CNS diseases such as Huntington's, Alzheimer's, Parkinson's, etc., see in particular column 25, line 55-column 26, line 26. Thus, Weiss clearly establishes that the treatment is to an individual having CNS damage or lesion as in claim 1.

Weiss is not limited to ventricular administration of growth factor. For example, Weiss teaches administration other than in the ventricle, see in particular oral administration, injection, injection cannula, timed release apparati at the desired site, see in particular column 25, line 20-column 26, line 15. New claim 1 as amended

recites parenteral administration. Parenteral administration refers to administration outside of the digestive tract. Weiss teaches that administration may be through injection and thus includes administration other than by the digestive tract. Moreover, Weiss teaches multiple methods of growth factor administration including via mechanisms in addition to direct in vivo administration. For example column 10, lines 23-column 11, line 4, teach that the administration may be via culture of cells with TGF-alpha, via transplantation of cells maintained or produced under such culture conditions, or via genetic manipulation of cells to provide the growth factor to the host either in vitro or in vivo. The claims further specify that preferred areas suitable for transplantation of such cells either supported by TGF-alpha or which produce TGF-alpha are to areas of CNS brain tissue including the striatum, adjacent to the ventricle (the subependymal zone), and to spinal cord tissue, see in particular column 12, line 53-column 13, line 41. Weiss et al., teach that the administration of the TGF-alpha growth factor can be by any method, including injection cannula, transfection of cells with growth hormone-expressing vectors, transplantation of cells maintained in TGF-alpha, via direct injection, and via timed release apparati which can administer substances at the desired site, see in particular column 25, lines 40-column 26, line 15. Moreover, Weiss teaches that the direct administration may be so as to provide proliferation and differentiation of the cells as described by the noted genetic modifications, or culture and transplantation methods provided. Such mechanisms and sites of interest include transplantation or delivery to basal gangia, caudate, putamen, nucleus basalis or substantia nigra, i.e., into the striatum as claimed, see in particular column 23, lines 4-21, column 26, lines 21-26 and 61-64. Also the compositions may be administered via oral administrations, see in particular column 25, lines 40-55. (Claims 33 and 63 are not limited to parenteral administration). Additionally it is noted that a desired site is in the striatum as noted at

column 26, lines 22-26 and 61-64. For treatment of spinal cord injury, MS or other deyelinating diseases growth factors would be delivered to spinal cord as in Examples 15-17. Further Example 44 teaches neural stem cell proliferation in spinal cord tissue from vertebral column, thoracic, and lumbar-sacral tissue and column 62 teaches mouse models of spinal cord injury and disease treatment via transplantation into lumbar lateral funiculus. Thus, Weiss acknowledges administration via various mechanisms, "outside the ventricles".

Claim 20 recites wherein the CNS tissue is in tissue culture. Weiss teach the proliferation of neural and glial cell precursors in vitro and further teach culture of such cells from a patient from in vivo tissue to culture with TGF-alpha, see in particular columns 22-23.

Claim 63 recites intrastriatal administration and claim 64 via continuous infusion. Weiss teaches methods and compositions for the treatment of Parkinson's disease where new stem cells are generated in the striatum via administration of neural stem cell progeny resulting from genetically modified or cultured stem cells stimulated via growth factors to the lateral ventricle or at the site of lesion, see in particular column 22, lines 10-18, column 26, lines 41-45 and column 60. Weiss also teaches where administration of the neural precursors/progeny may be administered at the lesion site, see in particular column 62, line 63-column 63, line 50 and hence injection. In addition, Weiss teaches infusion into the lateral ventricles for six consecutive days via continuous infusion, see in particular column 28, lines 1-9, 18-26, 60-67 and Example 27.

Further as to the mechanism of action of such administration, Weiss teaches that the neural stem cell progeny stimulated by TGF-alpha can migrate into regions that have been damaged as a result of injury or disease, see in particular column 26, lines 10-12. Weiss further teaches that in vivo infusion results in the induction of proliferation

migration and differentiation of neural stem cells and progenitor cells in vivo, see in particular column 27, lines 20-24.

Even though the reference does not ipsis verbis teach administration "outside the ventricles" the reference teachings provide for administration of the growth factors outside the ventricles because the reference teaches the relevant sites outside the ventricles that are to be treated by the neural precursor cells that are stimulated to proliferate, differentiate and migrate via TGF-alpha exposure. The cells may be provided via the alternative conventions of in vitro proliferation with TGF-alpha followed by subsequent transplantation to the site, transplantation of cells genetically modified to provide TGF-alpha to the relevant site, and direct administration of the growth factor in vivo, see in particular Summary of the Invention, column 10, line 23-67 and column 11, lines 40-66. The relevant intrastriatal site is clearly identified as the desired site to provide for replacement of dopaminergic neurons in Parkinson's disease. Thus the reference teaches that the direct in vivo administration may be via intrastriatal infusion and would provide for the necessary growth factor in the striatum or subependymal zone region "desired site" where proliferation to produce dopaminergic neurons is required. The reference teaches that that direct injection is appropriate to provide delivery at the desired site which is outside of the ventricle. Weiss teaches administration at the site of damage or lesion where promotion of growth, differentiation and migration of neural and glial cells would occur for the treatment of intrastriatal neurons in Parkinson's disease. Moreover, the reference teaches the desired site of spinal cord neurons and injection or administration to spinal cord neurons for treatment of spinal cord injury or multiple sclerosis. Further as noted above the administration via direct injection may be via injection cannula capable of providing continuous infusion. Thus, the reference teaches direct injection of the growth factor at the relevant site

outside the ventricle and into the striatum or spinal cord. The reference teaches that direct administration is suitable and avoids the noted problems associated with transplantation of heterologous cells in vivo, see in particular column 12-15. The reference teaches that administration via continuous infusion over six days as directed by Weiss can provide for the proliferative and migratory effects of the precursors either in vitro over multiple days or in vivo via injection over multiple days. While Weiss specifically exemplifies continuous infusion into the ventricles the reference teachings are not so limited. Weiss teaches injection and injection cannula for delivery at cumulative sites and durations so as to provide proliferation, differentiation and migration. Thus, the reference teachings anticipate the claimed invention. The art rejections have been alternatively set forth in a 103 rejection as the teachings are not ipsis verbis. However, the teachings apparently arise to that of anticipation as the reference is enabling to the artisan for practice of the claimed invention. The rejections above are not in conflict in that "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." In re Best, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977).

***Claim Rejections - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1-3, 5-8, 20, 33, and 63-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weiss et al., 5,980,885, filed June 7, 1995 and issued Nov. 9, 1999.

Applicants note that their invention requires lesion or damage in addition to administration outside of the ventricles. Applicant's note that administration to the ventricles is not effective to provide for attraction of neural progenitor cells as claimed. Applicant's argue the previous 102 rejection of record citing that Weiss fails to teach or suggest administration of TGF-alpha outside the ventricles to an individual having CNS damage or lesion.

Applicants arguments have been fully considered. While it is true that Weiss directs that a preferred embodiment of the invention is delivery of the growth factor to the ventricles, the Examiner notes that Weiss is not limited to a teaching of administration to the ventricles. Moreover, Weiss is directed to administration to patients with damage or lesion and for the purpose of attraction of neural progenitor cells to a site of damage or lesion in the CNS.

The teachings of Weiss are as set forth above.

While the Weiss patent fails to ipsis verbis teach administration of TGF-alpha, "outside the ventricles," via, "intrastriatal administration," and wherein the site is, "spinal cord tissue and spinal nerve root origins," such limitations are rendered obvious by the reference as a whole.

Weiss et al., teach administration of TGF-α to patients in vivo for the purpose of inducing in vivo proliferation, migration and differentiation of neural and/or glial cell precursors and for treatment of injuries and diseases of the nervous system including Huntington's, Alzheimer's, Parkinson's and other neurological disorders, see in particular Abstract, lines 5-7, column 25, line 20-column 26, line 64 and Examples 27-

30. In addition, the method may be used in areas of demyelination or autoimmune disease such as MS for proliferation of glial schwann, see in particular columns 24-25. The method is also disclosed for use in the replacement of neurons, for example as transplants or grafts, disclosed at column 23. Weiss further teaches that these effects may be achieved by direct administration, thus obviating particular problems associated with transplant, see in particular column 12-25 in regard to culture, modification and transplantation of cells and columns 25-29 for the alternative method of direct administration for production of the appropriate cells and treatment in vivo. The cells so produced may be generically used to replace damaged or missing neurons and/or glia, see in particular Abstract and column 25, lines 34-41. In particular Weiss teaches injection of growth factors to animals having CNS damages or lesion, see in particular column 22, lines 10-17. The method as amended is also directed to an individual having CNS damage or lesion. Weiss teaches administration to patients suffering from injury or damage to the CNS and for CNS diseases such as Huntington's, Alzheimer's, Parkinson's, etc., see in particular column 25, line 55-column 26, line 26. Thus, Weiss clearly establishes that the treatment is to an individual having CNS damage or lesion as in claim 1.

Weiss is not limited to ventricular administration of growth factor. For example, Weiss teaches administration other than in the ventricle, see in particular oral administration, injection, injection cannula, timed release apparati at the desired site, see in particular column 25, line 20-column 26, line 15. New claim 1 as amended recites parenteral administration. Parenteral administration refers to administration outside of the digestive tract. Weiss teaches that administration may be through

injection and thus includes administration other than by the digestive tract. Moreover, Weiss teaches multiple methods of growth factor administration including via mechanisms in addition to direct in vivo administration. For example column 10, lines 23-column 11, line 4, teach that the administration may be via culture of cells with TGF-alpha, via transplantation of cells maintained or produced under such culture conditions, or via genetic manipulation of cells to provide the growth factor to the host either in vitro or in vivo. The claims further specify that preferred areas suitable for transplantation of such cells either supported by TGF-alpha or which produce TGF-alpha are to areas of CNS brain tissue including the striatum, adjacent to the ventricle (the subependymal zone), and to spinal cord tissue, see in particular column 12, line 53-column 13, line 41. Weiss et al., teach that the administration of the TGF-alpha growth factor can be by any method, including injection cannula, transfection of cells with growth hormone-expressing vectors, transplantation of cells maintained in TGF-alpha, via direct injection, and via timed release apparati which can administer substances at the desired site, see in particular column 25, lines 40-column 26, line 15. Moreover, Weiss teaches that the direct administration may be so as to provide proliferation and differentiation of the cells as described by the noted genetic modifications, or culture and transplantation methods provided. Such mechanisms and sites of interest include transplantation or delivery to basal gangia, caudate, putamen, nucleus basalis or substantia nigra, i.e., into the striatum as claimed, see in particular column 23, lines 4-21, column 26, lines 21-26 and 61-64. Also the compositions may be administered via oral administrations, see in particular column 25, lines 40-55. (Claims 33 and 63 are not limited to parenteral administration). Additionally it is noted that a desired site is in the striatum as noted at column 26, lines 22-26 and 61-64. For treatment of spinal cord injury, MS or other deyelinating diseases growth factors would be delivered to spinal cord as in Examples

15-17. Further Example 44 teaches neural stem cell proliferation in spinal cord tissue from vertebral column, thoracic, and lumbar-sacral tissue and column 62 teaches mouse models of spinal cord injury and disease treatment via transplantation into lumbar lateral funiculus. Thus, Weiss acknowledges administration via various mechanisms, "outside the ventricles".

Claim 20 recites wherein the CNS tissue is in tissue culture. Weiss teach the proliferation of neural and glial cell precursors in vitro and further teach culture of such cells from a patient from in vivo tissue to culture with TGF-alpha, see in particular columns 22-23.

Claim 63 recites intrastriatal administration and claim 64 via continuous infusion. Weiss teaches methods and compositions for the treatment of Parkinson's disease where new stem cells are generated in the striatum via administration of neural stem cell progeny resulting from genetically modified or cultured stem cells stimulated via growth factors to the lateral ventricle or at the site of lesion, see in particular column 22, lines 10-18, column 26, lines 41-45 and column 60. Weiss also teaches where administration of the neural precursors/progeny may be administered at the lesion site, see in particular column 62, line 63-column 63, line 50 and hence injection. In addition, Weiss teaches infusion into the lateral ventricles for six consecutive days via continuous infusion, see in particular column 28, lines 1-9, 18-26, 60-67 and Example 27.

Further as to the mechanism of action of such administration, Weiss teaches that the neural stem cell progeny stimulated by TGF-alpha can migrate into regions that have been damaged as a result of injury or disease, see in particular column 26, lines 10-12. Weiss further teaches that in vivo infusion results in the induction of proliferation migration and differentiation of neural stem cells and progenitor cells in vivo, see in particular column 27, lines 20-24.

Weiss et al., fail to ipsis verbis teach administration "outside the ventricles", via "intrastriatal infusion" and to "spinal cord tissue and spinal nerve root origins".

However, Weiss renders obvious administration of the growth factors outside the ventricles because the reference teaches the relevant sites outside the ventricles that are to be treated by the neural precursor cells and that are stimulated to proliferate, differentiate and migrate via TGF-alpha exposure. The reference further teaches direct administration via oral administration, injection and injection cannula. The administration is in vivo. Alternatively the methods may be practiced indirectly via transplantation of cells treated in culture or genetically modified cells which produce the growth factor. However, the artisan recognizes that direct administration at the site circumvents the need for transplantation procedures. Thus, direct administration provides the advantage of being simple and avoids histocompatibility rejection via the host. The cells may alternatively be provided via the conventions of in vitro proliferation with TGF-alpha followed by subsequent transplantation to the site, transplantation of cells genetically modified to provide TGF-alpha to the relevant site, and direct administration of the growth factor in vivo, see in particular Summary of the Invention, column 10, line 23-67 and column 11, lines 40-66. The relevant intrastriatal site is clearly identified as the desired site to provide for replacement of dopaminergic neurons in Parkinson's disease. Thus the reference renders obvious that the direct in vivo administration may be via intrastriatal infusion and would provide for the necessary growth factor in the striatum or subependymal zone region "desired site" where proliferation to produce dopaminergic neurons is required. The reference teaches that that direct injection is appropriate to provide delivery at the desired site which is outside of the ventricle. Weiss teaches administration at the site of damage or lesion where promotion of growth, differentiation and migration of neural and glial cells would occur

for the treatment of intrastriatal neurons in Parkinson's disease. Moreover, the reference teaches the desired site of spinal cord neurons and injection or administration to spinal cord neurons for treatment of spinal cord injury or multiple sclerosis. Further as noted above the administration via direct injection may be via injection cannula capable of providing continuous infusion. Thus, the reference renders obvious direct injection of the growth factor at the relevant site outside the ventricle and into the striatum or spinal cord. The reference teaches that direct administration is suitable and avoids the noted problems associated with transplantation of heterologous cells in vivo, see in particular column 12-15. The reference teaches that administration via continuous infusion over six days as directed by Weiss can provide for the proliferative and migratory effects of the precursors either in vitro over multiple days or in vivo via injection over multiple days. While Weiss specifically exemplifies continuous infusion into the ventricles the reference teachings are not so limited. Weiss teaches injection and injection cannula for delivery at cumulative sites and durations so as to provide proliferation, differentiation and migration. Thus, the reference teachings render obvious the the claimed invention directed to continuous infusion. The artisan would expect positive results using the various modifications given the success of Weiss in providing treatment of Parkinson's disease and spinal cord injury as exemplified in the '885 patent. Thus, the cumulative references teachings render the claimed invention obvious to one of skill in the art. The art rejections have been alternatively set forth in a 103 rejection as the teachings are not ipsis verbis. However, the teachings apparently arise to that of anticipation as the reference is enabling to the artisan for practice of the claimed invention. The rejections above are not in conflict in that "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for

anticipation under 35 U.S.C. 102." In re Best, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977).

**Status of Claims**

10. No claims are allowed.

11. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.
December 1, 2003